

<b>U. S. PATENT AND TRADEMARK OFFICE U.S. DEPARTMENT OF COMMERCE</b>		<b>ATTORNEY'S DOCKET NUMBER</b>  ITR0041P
<b>TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371</b>		<b>U.S. APPLICATION NO. (If known, see 37 CFR 1.5)</b>  <b>10/576919</b>
<b>INTERNATIONAL APPLICATION NO.</b> PCT/EP2004/011683	<b>INTERNATIONAL FILING DATE</b> 15 October 2004	<b>PRIORITY DATE CLAIMED</b> 24 October 2003
<b>TITLE OF INVENTION</b> ORTHOGONAL GENE SWITCHES		
<b>APPLICANT(S) FOR DO/EO/US</b> Gennaro Ciliberto, Raffaele De Francesco, Daniela Fattori, Paola Gallinari, Olaf D. Kinzel, Uwe Koch, Ester Muraglia, Carlo Toniatti, Riccardo Cortese and Armin Lahm		
<p><b>Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:</b></p> <ol style="list-style-type: none"><li>1. <input checked="" type="checkbox"/> This is a <b>FIRST</b> submission of items concerning a filing under 35 U.S.C. 371.</li><li>2. <input type="checkbox"/> This is a <b>SECOND</b> or <b>SUBSEQUENT</b> submission of items concerning a filing under 35 U.S.C. 371.</li><li>3. <input type="checkbox"/> This is an express request to begin national examination procedures [35 U.S.C. 371(f)]. The submission must include items (5), (6), (9) and (21) indicated below.</li><li>4. <input type="checkbox"/> The US has been elected (PCT Article 31).</li><li>5. <input checked="" type="checkbox"/> A copy of the International Application as filed [35 U.S.C. 371(c)(2)]<ol style="list-style-type: none"><li>a. <input type="checkbox"/> is attached hereto (required only if not communicated by the International Bureau).</li><li>b. <input checked="" type="checkbox"/> has been communicated by the International Bureau.</li><li>c. <input type="checkbox"/> is not required, as the application was filed in the United States Receiving Office (RO/US).</li></ol></li><li>6. <input type="checkbox"/> An English language translation of the International Application as filed [35 U.S.C. 371(c)(2)].<ol style="list-style-type: none"><li>a. <input type="checkbox"/> is attached hereto</li><li>b. <input type="checkbox"/> has been previously submitted under 35 U.S.C. 154(d)(4).</li></ol></li><li>7. <input type="checkbox"/> Amendments to the claims of the International Application under PCT Article 19 [35 U.S.C. 371(c)(3)].<ol style="list-style-type: none"><li>a. <input type="checkbox"/> are attached hereto (required only if not communicated by the International Bureau).</li><li>b. <input type="checkbox"/> have been communicated by the International Bureau.</li><li>c. <input type="checkbox"/> have not been made; however, the time limit for making such amendments has NOT expired.</li><li>d. <input type="checkbox"/> have not been made and will not be made.</li></ol></li><li>8. <input type="checkbox"/> An English language translation of the amendments to the claims under PCT Article 19 [35 U.S.C. 371(c)(3)].</li><li>9. <input type="checkbox"/> An oath or declaration of the inventor(s) [35 U.S.C. 371(c)(4)].</li><li>10. <input type="checkbox"/> An English language translation of the annexes of the International Preliminary Examination Report under PCT Article 36 [35 U.S.C. 371(c)(5)].</li></ol> <p><b>Items 11 to 20 below concern other document(s) or information included:</b></p> <ol style="list-style-type: none"><li>11. <input type="checkbox"/> An Information Disclosure Statement under 37 CFR 1.97 and 1.98.</li><li>12. <input type="checkbox"/> An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.</li><li>13. <input type="checkbox"/> A preliminary amendment.</li><li>14. <input type="checkbox"/> An Application Data Sheet under 37 CFR 1.76.</li><li>15. <input type="checkbox"/> A substitute specification.</li><li>16. <input type="checkbox"/> A power of attorney and/or change of address letter.</li><li>17. <input checked="" type="checkbox"/> A computer-readable form of the sequence listing in accordance with PCT Rule 13ter.2 and 37 CFR 1.821 - 1.825.</li><li>18. <input type="checkbox"/> A second copy of the published International Application under 35 U.S.C. 154(d)(4).</li><li>19. <input type="checkbox"/> A second copy of the English language translation of the international application under 35 U.S.C. 154(d)(4).</li><li>20. <input type="checkbox"/> Other items or information:</li></ol>		

U.S. APPLICATION NO. (If known, see 37 CFR 1.53) <div style="font-size: 2em; font-weight: bold; transform: rotate(-5deg); position: absolute; left: 100px; top: 50px;">10/5/6929</div>		INTERNATIONAL APPLICATION NO. PCT/EP2004/011683		ATTORNEY'S DOCKET NUMBER ITR0041P	
The following fees are submitted:				CALCULATIONS	PTO USE ONLY
21. <input checked="" type="checkbox"/> Basic national fee.....\$300				\$300.00	
22. <input checked="" type="checkbox"/> Examination fee (37 CFR 1.492(c)) If the written opinion prepared by ISA/US or the international preliminary examination report prepared by IPEA/US indicates all claims satisfy provisions of PCT Article 33(1)-(4).....\$0 All other situations.....\$200				\$200.00	
23. <input checked="" type="checkbox"/> Search fee (37 CFR 1.492(b)) If the written opinion of the ISA/US or the international preliminary examination report prepared by IPEA/US indicates all claims satisfy provisions of PCT Article 33(1)-(4).....\$0 Search fee [37 CFR 1.445(a)(2)] has been paid on the international application to the USPTO as an International Searching Authority.....\$100 International Search Report prepared by an ISA other than the US and provided to the Office or previously communicated to the US by the IB .....\$400 All other situations.....\$500				\$400.00	
<b>TOTAL OF 21, 22 and 23=</b>				<b>\$900.00</b>	
<input type="checkbox"/> Additional fee for specification and drawings filed in paper over 100 sheets (excluding sequence listing or computer program listing filed in an electronic medium). The fee is \$250 for each additional 50 sheets of paper or fraction thereof.					
Total Sheets	Extra Sheets	Number of each additional 50 or fraction thereof (round up to a whole number)	RATE		
108 - 100 =	8 /50	0.16 = 1	X \$250.00	\$250.00	
Surcharge of \$130.00 for furnishing the oath or declaration later than 30 months from the earliest claimed priority date [37 CFR 1.492(e)].					
CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE		
Total Claims	39 - 20 =	19	X \$50.00	\$950.00	
Independent Claims	3 - 3 =	0	X \$200.00	\$0.00	
MULTIPLE DEPENDENT CLAIM(S) (if applicable)			+ \$360.00		
<b>TOTAL OF ABOVE CALCULATIONS (SUBTOTAL)</b>				<b>\$2,100.00</b>	
Processing fee of \$130.00 for furnishing the English translation later than 30 months from the earliest claimed priority date (37 CFR 1.492(f)).				+	
<b>TOTAL NATIONAL FEE</b>				<b>\$2,100.00</b>	
Fee for recording the enclosed assignment [37 CFR 1.21(h)]. The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). \$40.00 per property.				+	
<b>TOTAL FEES ENCLOSED</b>				<b>\$2,100.00</b>	
				Amount to be refunded:	
				Amount to be charged:	
a. <input type="checkbox"/> A check in the amount of \$ _____ to cover the above fees is enclosed. b. <input checked="" type="checkbox"/> Please charge my Deposit Account No. <u>13-2755</u> in the amount of <u>\$2,100.00</u> to cover the above fees. A duplicate copy of this sheet is enclosed. c. <input checked="" type="checkbox"/> The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to the Deposit Account No. <u>13-2755</u> . A duplicate copy of this sheet is enclosed.					
<b>NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive [37 CFR 1.137(a) or (b)] must be filed and granted to restore the International Application to pending status.</b>					
SEND ALL CORRESPONDENCE TO: <div style="border: 1px solid black; padding: 2px; display: inline-block;">Customer No. 000210</div>					
MERCK & CO., INC. Patent Department, RY60-30 P.O. Box 2000 126 East Lincoln Avenue Rahway, New Jersey 07065-0970			<div style="font-size: 1.5em; font-family: cursive; margin-bottom: 5px;">Heidi M. Struse</div> SIGNATURE		
DATE: <u>April 24, 2006</u>			Heidi M. Struse NAME		
PHONE #: <u>(732) 594-0238</u>			<u>50,288</u> REGISTRATION NUMBER		

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DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING  
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**International Appln No.:** PCT/EP2004/011683  
**International Filing Date:** 15 October 2004  
**Priority Date:** 24 October 2003  
**Title:** ORTHOGONAL GENE SWITCHES

**Inventors:** Gennaro Ciliberto, Raffaele De Francesco, Daniela Fattori,  
Paola Gallinari, Olaf D. Kinzel, Uwe Koch, Ester Muraglia,  
Carlo Toniatti, Riccardo Cortese and Armin Lahm

EXPRESS MAIL CERTIFICATE	
DATE OF DEPOSIT	<u>April 24, 2006</u>
EXPRESS MAIL NO.	<u>EV66060208345</u>
I HEREBY CERTIFY THAT THIS CORRESPONDENCE IS BEING DEPOSITED WITH THE UNITED STATES POSTAL SERVICE AS EXPRESS MAIL "POST OFFICE TO ADDRESSEE" ON THE ABOVE DATE IN AN ENVELOPE ADDRESSED TO COMMISSIONER FOR PATENTS P.O. BOX 1450, ALEXANDRIA, VIRGINIA 22313-1450.	
MAILED BY	<u>Lori Schepisi</u> DATE <u>4-24-06</u>